

extension of time is enclosed to extend the deadline to respond to the restriction requirement until February 13, 2001. Please enter the following Amendments and remarks.

AMENDMENT

IN THE CLAIMS

1. (Reiterated). A modified therapeutic peptide capable of forming a peptidase stabilized therapeutic peptide composed of between 3 and 50 amino acids, said peptide having a carboxy terminal amino acid, an amino terminal amino acid, a therapeutically active region of amino acids and a less therapeutically active region of amino acids, said peptide comprising:
a reactive group which reacts with amino groups, hydroxyl groups, or thiol groups on blood components to form a stable covalent bond thereby forming the peptidase stabilized therapeutic peptide wherein the reactive group is selected from the group consisting of succinimidyl and maleimido groups and wherein the reactive group is attached to an amino acid positioned in said less therapeutically active region of amino acids.
2. (Reiterated). The peptide of claim 1 wherein said therapeutically active region of amino acids includes said carboxy terminal amino acid and said reactive group is attached to said amino terminal amino acid.
3. (Reiterated). The peptide of claim 1 wherein said therapeutically active region of amino acids includes said amino terminal amino acid and said reactive group is attached to said carboxy terminal amino acid.
4. (Reiterated). The peptide of claim 1 wherein said therapeutically active region of amino acids includes said carboxy terminal amino acid and said reactive group is attached to an amino acid positioned between said amino terminal amino acid and said carboxy terminal amino acid.

5. (Reiterated). The peptide of claim 1 wherein said therapeutically active region of amino acids includes said amino terminal amino acid and said reactive group is attached to an amino acid positioned between said amino terminal amino acid and said carboxy terminal amino acid.

Please CANCEL Claim 6.

A1
7. (Amended). A method for protecting from peptidase degradation a therapeutic peptide sensitive to such peptidase degradation *in vivo*, said peptide comprising between 3 and 50 amino acids and having a carboxy terminus and an amino terminus and a carboxy terminal amino acid and an amino terminal amino acid, comprising:

- Sub B1**
- (a) modifying said peptide by coupling a reactive group to the carboxy terminal amino acid, to the amino terminal amino acid, or to an amino acid located between the amino terminal amino acid and the carboxy terminal amino acid, the reactive group being capable of forming a covalent bond *in vivo* with a reactive functionality on a blood component; and
 - (b) forming a covalent bond between said reactive group and a reactive functionality on a blood component to form a peptide-blood component conjugate, thereby protecting said peptide from peptidase degradation.

8. (Amended). A method according to claim 7, wherein the peptide-blood component conjugate is formed *in vivo*.

9. (Amended). A method according to claim 7, wherein the peptide-blood component conjugate is formed *ex vivo*.

Please CANCEL Claim 10.

A2

11. (Amended). A method according to claim 7, wherein said reactive group comprises a maleimide group.

12. (Amended). A method according to claim 7, wherein said reactive group is coupled to said peptide via a lysine and/or a linking group.

13. (Reiterated). A method according to claim 7, wherein said blood component is albumin.

14. (Reiterated). A method according to claim 7, wherein one or more of said amino acids is synthetic.

A3

15. (Amended). A method for protecting from peptidase degradation a therapeutic peptide sensitive to such peptidase degradation *in vivo*, said peptide comprising between 3 and 50 amino acids and having a therapeutically active region of amino acids and a less therapeutically active region of amino acids, comprising:

(a) identifying said therapeutically active region of amino acids;

(b) modifying said peptide at an amino acid included in said less therapeutically active region by coupling thereto a reactive group to said amino acid to form a modified peptide, such that said modified peptide has therapeutic activity, the reactive group being capable of forming a covalent bond *in vivo* with a reactive functionality on a blood component; and

(c) forming a covalent bond between said reactive entity and a reactive functionality on a blood component to form a peptide-blood component conjugate, thereby protecting said peptide from peptidase activity.

CONT
A3 16. (Amended). A method according to claim 15, wherein the peptide-blood component conjugate is formed *in vivo*.

17. (Amended). A method according to claim 15, wherein the peptide-blood component conjugate is formed *ex vivo*.

Please CANCEL Claims 18-20.

A4 21. (Amended). A method according to claim 15, wherein said peptide has a carboxy terminus, an amino terminus, a carboxy terminal amino acid and an amino terminal amino acid, and wherein step (b) further comprises:

(a) if said less therapeutically active region is located at the carboxy terminus of said peptide, then modifying said peptide at the carboxy terminal amino acid of said peptide; or

(b) if said less therapeutically active region is located at the amino terminus of said peptide, then modifying said peptide at the amino terminal amino acid of said peptide; or (c) if said less therapeutically active region is located at neither the amino terminus nor the carboxy terminus of said peptide, then modifying said peptide at an amino acid located between the carboxy terminus and the amino terminus.

22. (Amended). A method according to claim 15, wherein said reactive group is a maleimide group.

23. (Amended). A method according to claim 15, wherein said reactive group is coupled to said peptide via a linking group.

24. (Reiterated). A method according to claim 15, wherein said blood component is albumin.